UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/820,563	04/08/2004	Vernon Wong	D3136CON1CIP RE	8667

33197 7590 04/01/2009

STOUT, UXA, BUYAN & MULLINS LLP
4 VENTURE, SUITE 300
IRVINE, CA 92618

EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	PAPER NUMBER
1616	
MAIL DATE	DELIVERY MODE
04/01/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/820,563	WONG ET AL.	
	Examiner	Art Unit	
	JAMES H. ALSTRUM ACEVEDO	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/22/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-51* is/are pending in the application.

4a) Of the above claim(s) *20-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☒ Claim(s) *2* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :7/14/08; 4/4/05; 3/2/05; 10/29/04.

DETAILED ACTION

Claims 1-51 are pending. Claims 20-51 are withdrawn as being drawn to a non-elected invention. **Claims 1-19 are under examination in the instant office action**. The instant application is a reissue of U.S. Patent No. 6,369,116 (formerly application No. 09/221,002). Applicants are advised that a different Examiner is examining the instant application. The suspension of the instant application has ended and prosecution is reopened. Applicants' arguments submitted on May 22, 2006 are noted and were considered. Applicants' arguments did not address the rejection under §251 made in the previous office action, because, after an interview with Mr. William Dixon, Jr. (Special Program Examiner), Applicants appear to have anticipated suspension of the prosecution of the instant application in favor of prosecution of the divisional application 11/440,204.

Priority

The instant application is a reissue of U.S. Patent No. 6,369,116 (formerly application No. 09/221,002- filed on December 23, 1998), which is a continuation-in-part (CIP) of U.S. application No. 09/160,635 (now U.S. Patent No. 7,048,946), which is a continuation (CON) of 08/459,134 (now U.S. Patent No. 5,869,079). The instant application is ***not granted*** benefit of priority to parent 09/160,635, because the CIP parent does not provide support for a method of improving the post-operative success of glaucoma filtration surgery. There is no mention in the specification of the parent CIP of any method of glaucoma filtration surgery or the concept of improving the post-operative success of glaucoma filtration surgery. There is only a general statement indicating that the biodegradable implants disclosed in the parent CIP are generally suitable for

improving the treatment of ocular and other conditions by avoiding peaks and troughs of drug release (col. 9, line 67 through col. 10, line 2). The only surgery mentioned in the parent CIP is a passing reference to post-cataract surgery in col. 5, lines 6-10. It is also noted that the specification of the parent CIP does not provide support for release of a therapeutically active agent within a therapeutic dosage that does not vary by more than about 100% for a period of at least about three weeks. The only time periods mentioned in the parent CIP are periods of from about 3 days to 1 week for post-cataract surgery; about 4 to 6 weeks for the treatment of uveitis, and over 3-6 months for the treatment of cytomegalovirus infection (col. 5, lines 6-10). **For the aforementioned reasons, the effective filing date of the instant application is *December 23, 1998* (i.e. the filing date of application no. 09/221,002).**

Election/Restrictions

The restriction included in the office action mailed on April 7, 2006 is maintained. Applicants' election of claims 1-19 by original presentation remains in effect. Claims 20-51 remain withdrawn from consideration.

Reissue Applications

The reissue oath/declaration filed with this application is defective because the error which is relied upon to support the reissue application is not an error upon which a reissue can be based. See 37 CFR 1.175(a)(1) and MPEP § 1414.

Claims 1-19 are rejected as being based upon a defective reissue declaration under 35 U.S.C. 251 as set forth above. See 37 CFR 1.175. The declaration does not

assert an affirmative statement of the alleged errors. For example, the declaration states that the alleged error "may render the patent partially inoperative for claiming less than the patentee had a right to claim in the parent." The use of the verb "may" to qualify the alleged error(s) is not acceptable.

The nature of the defect(s) in the declaration is set forth in the discussion above in this Office action.

Claim Objections

Claim 2 is objected to because of the following informalities: the word "modulator" is misspelled as "modular" on line 2 of claim 2. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-3, 5, and 8-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shields ("Glaucoma Filtering Surgery," In A Study Guide for Glaucoma", 1982, pp 453-476) (IDS) in view of Ohtori et al. (U.S. Patent No. 5,501,856) (IDS) and Tice et al. (EP 0102265) (IDS), as evidenced by Miller et al. (*J. Biomed. Mater. Res.* 1977, *11*, pp 711-719) (IDS).

Applicant Claims

Applicants claim a method for improving the post-operative success of glaucoma filtration surgery comprising (i) introducing proximally to the surgical site an implant comprising (a) from about 40 to about 80 % w/w of dexamethasone and (b) polylactate glycolic acid copolymer (PLGA) in an amount of at least about 20% w/w, wherein the dexamethasone is released within a therapeutic dosage which does not vary by more than about 100% for a period of at least about three weeks.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Shields teaches that glaucoma filtering surgery is the most frequently used to treat open-angle forms of glaucoma in adults and comprises the creation of an opening, or fistula, at the lumbus which permits aqueous humor to drain from the anterior chamber (pg. 454). The formation of a fistula necessarily requires formation of an opening into the sclera, because the sclera is the outermost protective layer of the eye. Generally before the fistula is made anesthesia is used (pg. 455). Some surgeons prefer making a beveled incision into the anterior chamber at the limbus as a route for injecting liquid at the end of the procedure (Id.). Surgeons then undertake the critical step of making a conjunctival flap (i.e. a scleral flap) followed by additional steps set forth in Figure 31.2 of (i) blunt dissection of Tenon's capsule, (ii) partial excision of Tenon's capsule, (iii) retraction of conjunctival flap over cornea with a moist foam sponge, (iv) closure of the conjunctival flap, (v) injection of balanced salt solution into the anterior chamber with elevation of the conjunctival flap (pg. 455, Figure 31.2 A-F). **Postoperative management typically involves topical mydriatic-cycloplegic and antibiotic therapy for the first 2-3 weeks in addition to the use of a topical corticosteroid to reduce scar formation of the filtering bleb** (pg. 458). **Implants are sometimes utilized in full-thickness and guarded filtering operations to maintain patency of the drainage** (pg. 465). Late postoperative complications may result from t**he filtering bleb becoming cystic and scarred down** or from closure of the fistula (pg. 468) due to the proliferation of episcleral or endothelial tissue. Other late post-operative complications include **bacterial infections** (e.g. endophthalmitis) (pg. 469).

Ohtori teaches controlled-release pharmaceutical preparations for **intra-ocular implant that are applied to the interior of the eye after a surgical operation for**

disorders, including glaucoma, wherein the pharmaceutical preparation includes an **anti-inflammatory agent and/or a proliferative antagonist** (title; abstract; col. 1, lines 6-18). Ohtori exemplifies **implants comprising 50% w/w dexamethasone m-sulfobenzoate sodium salt** (i.e. a corticosteroid anti-inflammatory) and polylactic acid, which in some embodiments comprises polylactic acid of two different average molecular weights (i.e. **Mn = 3200 or 5900**) (col. 3, lines 29-60). **Suitable number average molecular weights for the polylactic acid in Ohtori's preparations can range from about 2000 to about 4000 or from about 5000 to about 7000** (col. 2, lines 20-32 and 43-56). A number average molecular weight of about 5000 reads on a number average molecular weight of about 10 kD. Ohtori also exemplifies **implants comprising 5-fluorouracil an anti-proliferative agent** (col. 4, line 17 through col. 5, line 32). It is the Examiner's position that 5-fluorouracil reads on a hydrophilic modulator.

Tice teaches controlled-release anti-inflammatory microcapsules comprising an **anti-inflammatory in an amount preferably from 1-75% w/w** (title; abstract; pg. 3, line 20 through pg. 4, line 10; claims 2 and 8) and a biodegradable biocompatible polymer matrix (e.g. **copolymers of d,l-lactic acid and glycolic acid**) (pg. 4, lines 12-29; claims 3, 9, and 24) that may be used **to treat inflammation which arises from ophthalmic diseases** (pg. 9, lines 8-16). **Preferred anti-inflammatories include dexamethasones** (pg. 3, line 20 through pg. 4, line 10; claims 2 and 8).

Miller teaches that **the degradation rates of oral resorbable implants of polymers of lactic acid and glycolic acid can be varied from 2 weeks to 6 months by varying the relative amount of polylactic acid (PLA) and polyglycolic acid (PGA) in the polymer**. A PLA homopolymers had the longest degradation rate of 6.1 months

whereas a 100% PGA homopolymers had a degradation rate of 5 months and a 50:50 PGA:PLA copolymer had a degradation rate of 1 week (pg. 711, summary)

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Shields does not teach glaucoma filtration surgery comprising the insertion of an implant comprising dexamethasone and a polylactate glycolic acid copolymer. This deficiency is cured by the teachings of Ohtori and Tice. Miller was provided merely to demonstrate that it was well known in the art that varying the ratio of PLA and PGA in copolymers can be used to control the rate of polymer degradation and thus, drug release.

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to modify the teachings of Shields to include a step of implanting biodegradable biocompatible microparticles made from a copolymer of lactic acid and glycolic acid comprising an anti-inflammatory corticosteroid, such as dexamethasone, and/or an anti-proliferative, such as 5-fluorouracil, because typical post-operative management of glaucoma filtering surgery involves the administration of anti-inflammatory corticosteroids. Furthermore, it would have been prima facie obvious, because long-term complications of glaucoma filtering surgery include scarring and fistula closure due to the proliferation of episcleral and epithelial tissue. An ordinary skilled artisan would have been motivated to modify the teachings of Shields to improve the success of glaucoma filtering surgery, because common long-term complications include scarring and fistula closure due to the

proliferation of episcleral and epithelial tissue, which are typically treated by the administration of steroids (e.g. dexamethasone) to prevent scarring and anti-proliferative agents to prevent cell proliferation (e.g. 5-fluorouracil). An ordinary skilled artisan would have had a reasonable expectation of success in modifying the teachings of shields, because dexamethasone and 5-fluorouracil are conventional ophthalmologically suitable drugs used to manage post-glaucoma filtering surgery patient care and the implant taught by Ohtori and Tice are made from biodegradable biocompatible polymers taught as being suitable for ophthalmologic procedures. Regarding the molecular weight of the polymer matrix, molecular weight is a result effective parameter that an ordinary skilled artisan would vary to tune the properties of polymeric materials. Thus, absent a showing of unexpected results it would have been prima facie obvious to modify the average molecular weight of a copolymer of lactic acid and glycolic acid to obtain a polymer matrix exhibiting the desired release properties. Regarding the release rate, it is prima facie obvious that variation of the relative amount of PLA and PGA in a copolymer matrix would permit the ordinary skilled artisan to tune the drug release rate based upon the polymer matrix rate of degradation, as evidenced by Miller. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Claims 6-7 and 18-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shields ("Glaucoma Filtering Surgery," In A Study Guide for Glaucoma", 1982, pp 453-476) (IDS) in view of Ohtori et al. (U.S. Patent No.

5,501,856) (IDS) and Tice et al. (EP 0102265) (IDS), as evidenced by Miller et al. (*J. Biomed. Mater. Res.* 1977, *11*, pp 711-719) (IDS) as applied to claims 1-3, 5, and 8-17 above, and further in view of Cagle et al. (U.S. Patent No. 5,631,004).

Applicant Claims

Applicants claim a method for improving the post-operative success of glaucoma filtration surgery comprising as described above wherein the release modulator is a water soluble antibiotic (e.g. ciprofloxacin) or wherein the release modulator is hydroxypropyl methylcellulose.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Shields, Ohtori, Tice, and Miller are set forth above.

Cagle teaches **sustained release antibiotic compositions for ophthalmic surgical procedures** that are suitable to ensure a sterile field of surgery during intraocular surgical procedures **or to prevent post-surgical infections** (title; abstract; col. 1, lines 5-10). **Preferred antibiotics are quinolones, such as ciprofloxacin** (col. 2, lines 56-67).

Cagle teaches that the invented compositions may also comprise polymers capable of forming a solid or viscous gel that are ophthalmologically suitable and ensure an adequate residence time of the antibiotics in the eye include hydroxypropyl methylcellulose.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Shields/Ohtori/Tice lacks the express teaching of implants comprising antibiotics and/or hydroxypropyl methylcellulose. These deficiencies are cured by Cagle.

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to modify the teachings of Shields/Ohtori/Tice to utilize implants comprising antibiotics, such as ciprofloxacin, because Shields teaches that the post-operative care after glaucoma filtration surgery includes the application of antibiotics and identifies that long post-operative complications include bacterial infections. An ordinary skilled artisan would have been motivated to include antibiotics such as ciprofloxacin in the method of Shields as modified by Ohtori/Tice, because antibiotics would reduce the likelihood of late post-operative infections, which is a typical late post-operative complication after glaucoma filtration surgery. An ordinary skilled artisan would have had a reasonable expectation of successfully including ciprofloxacin in the method of Shields as modified by Ohtori/Tice and the teachings of Cagle, because it is suitable for ophthalmic application and Cagle's methods is designed for sustained (i.e. longer term release) of antibiotics.

It would have been prima facie obvious to include hydroxypropyl methylcellulose in the method of Shields as modified by Ohtori/Tice, because it is a polymer suitable for ophthalmic applications and is recognized as being suitable in ensure an adequate residence time of antibiotic in the eye. An ordinary skilled artisan would have been motivated to include hydroxypropyl methylcellulose, because it would help ensure that

antibiotic would remain in the eye long enough to kill bacteria and prevent bacterial infection. An ordinary skilled artisan would have had a reasonable expectation of including hydroxypropyl methylcellulose, because it is art-recognized as being suitable for ophthalmic application and in controlling the release of drug in the eye during or after surgery. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Conclusion

Claim 2 is objected. Claims 1-19 are rejected. Claims 20-51 are withdrawn from consideration. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner is on a flexible schedule, but can normally be reached on M-F ~10am~5:30 pm, and Saturdays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

J.H.A.-A.
Patent Examiner
Technology Center 1600

/Johann R. Richter/

Supervisory Patent Examiner, Art Unit 1616